CLAIMS

1. A method for treating cerebral ischemia comprising administering a compound capable of depleting mast cells or a compound inhibiting mast cells degranulation to a human in need of such treatment.

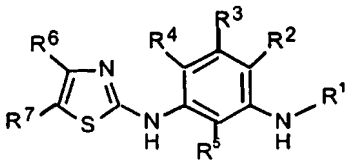
2. A method according to claim 1 for treating for treating cerebral ischemia comprising administering a c-kit inhibitor to a human in need of such treatment.

3. A method according to claim 2, wherein said c-kit inhibitor c-kit inhibitor is a non-toxic, selective and potent c-kit inhibitor wherein it is unable to promote death of IL-3 dependent cells cultured in presence of IL-3.

4. A method according to claim 1 or 3 wherein said inhibitor is selected from the group consisting of :

- 2-(3-amino)arylamino-4-aryl-thiazoles,
- pyrimidine derivatives, more particularly N-phenyl-2-pyrimidine-amine derivatives,
- indolinone derivatives, more particularly pyrrol-substituted indolinones,
- monocyclic, bicyclic aryl and heteroaryl compounds,
- and quinazoline derivatives.

5. A method according to claim 4, wherein said c-kit inhibitor is selected from compounds belonging to the 2-(3-amino)arylamino-4-aryl-thiazoles of **formula III**:



FORMULA III

wherein R^1 is :

a) a linear or branched alkyl group containing from 1 to 10 carbon atoms optionally substituted with at least one heteroatom, notably a halogen selected from I, Cl, Br and F, or bearing a pendant basic nitrogen functionality;

b) an aryl or heteroaryl group optionally substituted by an alkyl or aryl group optionally substituted with an heteroatom, notably a halogen selected from I, Cl, Br and F or bearing a pendant basic nitrogen functionality;

c) a sulfonyl or a -SO2-R group wherein R is an alkyl, aryl or heteroaryl substituted with an heteroatom, notably a halogen selected from I, Cl, Br and F or bearing a pendant basic nitrogen functionality;

d) a -CO-NH-R, –CO-R, -CO-OR or a -CO-NRR' group, wherein R and R' are independently chosen from H or an aryl, heteroaryl, alkyl and cycloalkyl group optionally substituted with at least one heteroatom, notably a halogen selected from I, Cl, Br and F, or bearing a pendant basic nitrogen functionality;

R^2 is hydrogen, halogen or a linear or branched alkyl group containing from 1 to 10 carbon atoms, trifluoromethyl or alkoxy;

R^3 is hydrogen, halogen or a linear or branched alkyl group containing from 1 to 10 carbon atoms, trifluoromethyl or alkoxy;

R^4 is hydrogen, halogen or a linear or branched alkyl group containing from 1 to 10 carbon atoms, trifluoromethyl or alkoxy;

R^5 is hydrogen, halogen or a linear or branched alkyl group containing from 1 to 10 carbon atoms, trifluoromethyl or alkoxy;

R^6 is one of the following:

(i) an aryl group such as phenyl or a substituted variant thereof bearing any combination, at any one ring position, of one or more substituents such as halogen, alkyl groups containing from 1 to 10 carbon atoms, trifluoromethyl, and alkoxy;

(ii) a heteroaryl group such as a 2, 3, or 4-pyridyl group, which may additionally bear any combination of one or more substituents such as halogen, alkyl groups containing from 1 to 10 carbon atoms, trifluoromethyl and alkoxy;

(iii) a five-membered ring aromatic heterocyclic group such as for example 2-thienyl, 3-thienyl, 2-thiazolyl, 4-thiazolyl, 5-thiazolyl, which may additionally bear any combination of one or more substituents such as halogen, an alkyl group containing from 1 to 10 carbon atoms, trifluoromethyl, and alkoxy,

iv) H, an halogen selected from I, F, Cl or Br; NH2, NO2 or SO2;

and R^7 is one of the following:

(i) an aryl group such as phenyl or a substituted variant thereof bearing any combination, at any one ring position, of one or more substituents such as halogen, alkyl groups containing from 1 to 10 carbon atoms, trifluoromethyl, and alkoxy;

(ii) a heteroaryl group such as a 2, 3, or 4-pyridyl group, which may additionally bear any combination of one or more substituents such as halogen, alkyl groups containing from 1 to 10 carbon atoms, trifluoromethyl and alkoxy;

(iii) a five-membered ring aromatic heterocyclic group such as for example 2-thienyl, 3-thienyl, 2-thiazolyl, 4-thiazolyl, 5-thiazolyl, which may additionally bear any combination of one or more substituents such as halogen, an alkyl group containing from 1 to 10 carbon atoms, trifluoromethyl, and alkoxy.

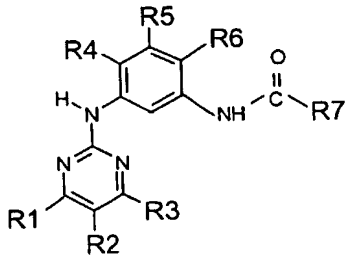
iv) H, an halogen selected from I, F, Cl or Br; NH2, NO2 or SO2.

6. A method according to one of claims 3 to 5, wherein said c-kit inhibitor is an inhibitor of activated c-kit.

7. A method according to claim 6, wherein said inhibitor is capable of inhibiting constitutively activated-mutant c-kit.

8. A method according to one of claims 3 to 5, wherein said activated c-kit inhibitor is capable of inhibiting SCF-activated c-kit.

9. A method according to claim 4, wherein said inhibitor is selected from the group consisting of N-phenyl-2-pyrimidine-amine derivatives having the formula II :



Wherein R1, R2 and R3 are independently chosen from H, F, Cl, Br, I, a C1-C5 alkyl or a cyclic or heterocyclic group, especially a pyridyl group;

R4, R5 and R6 are independently chosen from H, F, Cl, Br, I, a C1-C5 alkyl, especially a methyl group;

and R7 is a phenyl group bearing at least one substituent, which in turn possesses at least one basic site, such as an amino function.

10. A method according to claim 9, wherein said inhibitor is the 4-(4-méhylpipérazine-1-ylméthyl)-N-[4-méthyl-3-(4-pyridine-3-yl)pyrimidine-2 ylamino)phényl]-benzamide.

11. A method for treating and/or preventing or delaying renal cerebral ischemia comprising administering to a human in need of such treatment a compound that is a selective, potent and non toxic inhibitor of activated c-kit obtainable by a screening method which comprises :

a) bringing into contact (i) activated c-kit and (ii) at least one compound to be tested; under conditions allowing the components (i) and (ii) to form a complex,

b) selecting compounds that inhibit activated c-kit,

c) testing and selecting a subset of compounds identified in step b), which are unable to promote death of IL-3 dependent cells cultured in presence of IL-3.

12. A method according to claim 11, wherein the screening method further comprises the step consisting of testing and selecting a subset of compounds identified in step b) that are inhibitors of mutant activated c-kit, which are also capable of inhibiting SCF-activated c-kit wild.

13. A method according to claim 11, wherein activated c-kit is SCF-activated c-kit wild in step a).

14. A method according to one of claims 11 to 12, wherein putative inhibitors are tested at a concentration above 10 μM in step a).

15. A method according to one of claims 11 to 14, wherein IL-3 is preferably present in the culture media of IL-3 dependent cells at a concentration comprised between 0.5 and 10 ng/ml, preferably between 1 to 5 ng/ml.

16. A method according to one of claims 11 to 15, wherein IL-3 dependent cells are selected from the group consisting of mast cells, transfected mast cells, BaF3 and IC-2.

17. A method according to one of claims 11 to 16, wherein the extent to which component (ii) inhibits activated c-kit is measured *in vitro* or *in vivo*.

18. A method according to one of claims 11 to 17, further comprising the step consisting of testing and selecting compounds capable of inhibiting c-kit wild at concentration below 1 μM.

19. A method according to one of claims 11 to 18, wherein the inhibition of mutant-activated c-kit and/or c-kit wild is measured using standard biochemical techniques such as immunoprecipitation and western blot.

20. A method according to one of claims 11 to 19, wherein the amount of c-kit phosphorylation is measured.

21. A method according to one of claims 11 to 20, wherein identified and selected compounds are potent, selective and non-toxic c-kit wild inhibitors.

22. A method for treating and/or preventing or delaying cerebral ischemia comprising administering to a human in need of such treatment a c-kit inhibitor obtainable by a screening method comprising :

a) performing a proliferation assay with cells expressing a mutant c-kit (for example in the transphosphorylase domain), which mutant is a permanent activated c-kit, with a plurality of test compounds to identify a subset of candidate compounds targeting activated c-kit, each having an IC50 < 10 μM, by measuring the extent of cell death,

b) performing a proliferation assay with cells expressing c-kit wild said subset of candidate compounds identified in step (a), said cells being IL-3 dependent cells cultured in presence of IL-3, to identify a subset of candidate compounds targeting specifically c-kit,

c) performing a proliferation assay with cells expressing c-kit, with the subset of compounds identified in step b) and selecting a subset of candidate compounds targeting c-kit wild, each having an IC50 < 10 μM, preferably an IC50 < 1 μM, by measuring the extent of cell death.

23. A method according to claim 22, wherein the extent of cell death is measured by 3H thymidine incorporation, the trypan blue exclusion method or flow cytometry with propidium iodide.

24. A method according to one of claims 1 to 23 for preventing, delaying the onset and/or treating cerebral ischemia in human including treating hypoxic-ischemic encephalopathy induced by stroke, traumatic brain injury such as cerebral edema and embolic or thromboembolic occlusions of cerebral arteries, and ischemic insults following reperfusion.

25. A method according to one of claims 1 to 24 for preventing the onset or development of nerve cells damages few hours following either the cause of the ischemia or before, during and after reperfusion.

26. Use of a c-kit inhibitor to manufacture a medicament for treating for preventing, delaying the onset and/or treating cerebral ischemia including hypoxic-ischemic encephalopathy induced by stroke, traumatic brain injury such as cerebral edema and embolic or thromboembolic occlusions of cerebral arteries, and ischemic insults following reperfusion.